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EXAMINER

FORMAN, BETTY J

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7

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/497,269

Applicant(s)

YU ET AL.

Examiner

BJ Forman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 January 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 21-25 and 28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20, 26 and 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2. 6) ☐ Other: _____

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DETAILED ACTION

1. Applicant's election with traverse of Group I in Paper No. 6 is acknowledged. The traversal is on the grounds(s) that because the glucose analyte of Group II is a species of the analyte of Group I the groups are not distinct. Upon reconsideration and in view of Applicant's arguments, Groups I and II have been rejoined. Applicant further argues that it would not be undue burden to examine the claims of groups III and IV along with groups I and II. However, it is maintained that undue burden would be required to examine the claims of groups III and IV along with claims of groups I and II as evidenced by the fact that the claims of groups I, II, III and IV have acquired a separate status in the art as recognized by their different classifications as recognized by their divergent subject matter and because a search of the subject matter of invention I and II would not be co-extensive with a search of inventions III and IV. The inventions of groups I and II would require a search of redox-reaction zones and enzyme-containing test strips while the inventions of group III would require extensive search of test strips and test strip applications and the invention of group IV would require extensive search of instruments for analyzing physiological samples.

The restriction requirement for groups III and IV is still deemed proper and is therefore made FINAL.

Claims 1-20, 26 and 27 are under prosecution.

Specification

2. The disclosure is objected to because of the following informalities:

On pages 10-11 of the Specification, Applicant incorporates by reference co-pending application titled "Sample Detection to Initiate Timing of an Electrochemical Assay" (Attorney Docket No. LFS-77). The Specification does not provide a Serial No. for the co-pending

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application . The PALM database was searched for the Attorney Docket No. and for an application having this title filed by the inventors of the instant invention. However, the PALM database did not contain either the Attorney Docket No. or an application filed by the instant inventors having the given title. Therefore, the specification is objected to because information incorporated by reference is not described (see MPEP, § 608.01(p) I, 1).

Applicant is reminded that new matter may not be added to the Specification.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

First paragraph of 35 U.S.C. 112: Enablement

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to a test strip wherein said strip is present in an automated instrument (Claim 26) and a method for determining the concentration of an analyte employing an automated instrument (Claim 27). While the specification is enabling for the test strip and the method for determining concentration of an analyte, the specification does not enable one skilled in the art to which it pertains or with which it is most nearly connected to make or use the invention as claimed. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a

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disclosure does not satisfy the enablement requirements and whether undue experimentation would be required to make and use the claimed invention (see *In re Wands*, 858 F. 2d 731, 737, 8 USPQ 2d 1400, 1404, 1988). These factors include but are not limited to:

Breadth of the Claims

Claim 26 is drawn to the electrochemical test strip of Claim 1 wherein the test strip is present in an automated instrument. The claim is written so broadly so as to encompass an enormous genus of instruments. For example, the claimed automated instruments encompasses microscopes, computers, scintillation counters, autoclaves, centrifuges, thermocyclers, incubators and etc. The specification teaches the electrochemical test strip (page 4, lines 15-24 and Fig. 1 and 2). The specification also teaches that electrochemical signal measurement and analyte derivation steps are performed in automated devices designed to work with the test strip (page 10, lines 22-27). However, the specification does not describe the broadly claimed instruments.

Claim 27 is drawn to the method for determining concentration of an analyte wherein said method comprises employing an automated instrument. The claim is written so broadly so as to encompass an enormous genus of instruments. For example, the claimed automated instruments employable in the method of Claim 16 encompasses microscopes, computers, scintillation counters, autoclaves, centrifuges, thermocyclers, incubators and etc. The specification teaches a method for determining concentration of an analyte (page 9, line 20- page 10, line 7). The specification also teaches that analyte concentration is determined by measurement of an electrochemical signal wherein the measurement and analyte derivation steps are performed in automated devices designed to work with the test strip (page 10, lines 22-27). However, the specification does not describe the broadly claimed instruments.

The specification teaches that a representative device is described in a co-pending application titled "Sample Detection to Initiate Timing of an Electrochemical Assay" having the

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Attorney Docket No. LFS-77 which Applicant incorporates by reference. However, the incorporated reference is not obtainable by the examiner because neither the docket number nor an application by the instant inventor having the title is found in PALM. Therefore, the information which Applicant incorporates by reference is not adequately described so as to describe the broadly claimed invention.

Nature of the Invention

The Claim 26 is drawn to the electrochemical test strip present in an automated instrument). The claimed automated instruments encompass an enormous genus of instruments wherein a test strip may be present. The nature of the invention is such that an automated instrument containing test strips encompasses a very large number of instruments each having a large number of structural components wherein a test strip is present. For example, the test strip could be present within a microscope slide holder of a microscope for automated detection of the strip; the test strip could be present in a specially designed slot within an automated centrifuge; and the test strip could be present in a sealed environment within an automated incubator for automated environmental control of the test strip.

Claim 27 is drawn to a method for determining concentration of an analyte employing an automated instrument. The claimed automated instruments encompass an enormous genus of instruments which perform a very large variety of functions and method steps. The nature of the invention is such that the method for determining concentration of an analyte could employ a very large number of instruments each potentially having a number of functions for employment in the method. For example, the instrument could comprise an automated microscope for automated signal detection; the instrument could comprise an automated scintillation counter for automated quantification of radioactive signal; and the instrument could comprise an incubator for automated environmental and temperature control of the redox reaction.

The specification teaches a method for determining concentration of an analyte (page 9, line 20-page 10, line 7). The specification also teaches that analyte concentration is determined by measurement of an electrochemical signal wherein the measurement and analyte derivation steps are performed in automated devices designed to work with the test strip (page 10, lines 22-27). While the specification teaches measurement and derivations are performed in an automated device, the specification does not teach structural components wherein the test strip is present and the specification does not teach functional components of the automated instrument that would enable one skilled in the art to make and use the automated instruments as claimed.

Existence of Working Examples

The claims are drawn to the electrochemical test strip present in an automated instrument (Claim 26) and a method for determining concentration of an analyte employing an automated instrument (Claim 27). The claimed automated instruments encompasses an enormous genus of instruments which perform a very large variety of functions. The specification teaches that analyte concentration is determined by measurement of an electrochemical signal wherein the measurement and analyte derivation steps are performed in automated devices designed to work with the test strip (page 10, lines 22-27). The specification also teaches a method for determining concentration of an analyte (page 9, line 20-page 10, line 7) wherein the analyte concentration is determined by measurement of an electrochemical signal wherein the measurement and analyte derivation steps are performed in automated devices designed to work with the test strip (page 10, lines 22-27). However, the specification does not provide working examples of the claimed instruments.

The specification teaches that a representative device is described in a co-pending application titled "Sample Detection to Initiate Timing of an Electrochemical Assay" having the

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Attorney Docket No. LFS-77 which Application incorporates by reference. However, the incorporated reference is not obtainable by the examiner because neither the docket number nor an application by the instant inventor having the title are found in PALM.

Working examples of the claimed instruments would minimally include structural and functional components of the instruments. Additionally, working examples would describe a relationship between the structural and functional components of the automated instruments and the test strip. Further more, working examples would include a teaching of the functionality of the instruments as applicable to the claimed method of determining analyte concentrations. While the specification teaches measurement and derivations is performed in an automated device, the specification does not teach working examples of the claimed invention the teaching of which would minimally include structural and functional components of the instruments. Therefore, the specification does not provide working examples of the claimed invention which would enable one of ordinary skill in the art to make and use the invention as claimed.

Quantity of Experimentation Required

The claims are drawn to the electrochemical test strip present in an automated instrument (Claim 26) and a method for determining concentration of an analyte employing an automated instrument (Claim 27). The claimed automated instruments encompasses an enormous genus of instruments which perform a very large variety of functions. In view of the breadth of the claims being drawn to an enormous genus of instruments each potentially having a variety of functions; in view of the nature of the invention which requires specific structural components wherein a test strip is present and specific function components whereby analyte concentration is determined; in view of the lack of teaching of the specific structural and functional components; and in view of the lack of working examples of the

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broadly claimed invention, it would require undue experimentation for one skilled in the art to make and use the invention as claimed.

35 U.S.C. 112: Indefinite

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-20, 26 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-5 and 26 are indefinite in Claim 1, line 3 for the recitation "said first and second electrodes" because the recitation lacks proper antecedent basis in the "working and reference electrodes" of line 2. It is suggested that Claim 1 be amended to provide proper antecedent basis e.g. replace "first and second" with "working and reference".

b. Claims 6-11 are indefinite in Claim 6, line 3 for the recitation "said first and second electrodes" because the recitation lacks proper antecedent basis in the "working and reference electrodes" of line 2. It is suggested that Claim 6 be amended to provide proper antecedent basis e.g. replace "first and second" with "working and reference".

c. Claims 12-15 are indefinite in Claim 12, line 5 for the recitation "said first and second electrodes" because the recitation lacks proper antecedent basis in the "working and reference electrodes" of line 3. It is suggested that Claim 12 be amended to provide proper antecedent basis e.g. replace "first and second" with "working and reference".

d. Claims 16-20 and 27 are indefinite in Claim 16, line 6 for the recitation "said first and second electrodes" because the recitation lacks proper antecedent basis in the "working and reference electrodes" of line 5. It is suggested that Claim 16 be amended to provide proper antecedent basis e.g. replace "first and second" with "working and reference".

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e. Claims 16-20 and 27 are indefinite in Claim 16 because the claim is drawn to a method of determining concentration of an analyte, but the claims do not recite method steps for determining concentration. Claim 16 is further indefinite in (c) because “relating” is a non-specific relational term. Therefore the relationship between the signal and analyte in undefined. Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter the claims encompass as well as make clear the subject matter from which others would be precluded. *Ex parte Erlich*, 3 USPQ2d 1011 at 6. It is suggested that Claim 16 be amended to recite positive and active method steps for determining concentration and to define the relationship between the signal and the analyte e.g. replace “relating” with “measuring” and replace “the amount” with “to thereby determine the concentration” (specification, page 10, lines 22-24).

f. Claim 26 is indefinite for the recitation “wherein said strip is present in an automated instrument” because it is unclear how the recitation limits the structural components of the test strip of Claim 1. The recitation is further indefinite because it suggests that a physical relationship exists between the test strip and the automated instrument. However, a physical relationship is not defined. It is suggested that the claim be amended to define the physical relationship and to recite structural limitations of the test strip.

g. Claim 27 is indefinite for the recitation “employing an automated instrument” because the recitation does not recite positive and active method steps for “employing” the instrument. Therefore, it is unclear what functions the instrument performs and it is unclear at what method steps the instrument is employed. It is suggested that the claim be amended to recited positive and active method steps for employing the automated instruments as described in the specification e.g. measuring and derivatizing (page 10, lines 19-27)

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Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 1-14, 16-20, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over McAleer et al (U.S. Patent No. 5,708,247, issued 13 January 1998) in view of Mizutani et al (Analytica Chimica Acta, 1998, 364: 173-179) and Backhaus et al (U.S. Patent No. 5,869,001, issued 9 February 1999).

Regarding Claim 1, McAleer et al teach an electrochemical test strip comprising: a reaction zone defined by opposing working and reference electrodes separated by a spacer layer wherein at least one of the electrodes has a surface modified with a homogenous surface modification layer; and a redox reagent system in said reaction zone, said redox reagent system comprising at least one enzyme and a mediator (Column 2, lines 39-57) but they do not teach the modification layer comprises self assembling molecules having a first sulfhydryl end group and a second sulfonate end group. Mizutani et al teach a similar test strip comprising a reaction zone defined by working and reference electrodes, wherein the working electrode has a surface modified with a homogenous surface modification layer made up of self assembling molecules (page 174, last paragraph); and a redox reagent system present in said reaction zone comprising at least one enzyme and a mediator (page 174, last paragraph-page 175, second paragraph and Fig. 1) wherein the self-assembling molecules have a first sulfhydryl end group and a second carboxylic acid end group where said sulfhydryl and carboxylic acid end groups are separated by a lower alkyl linker group i.e. mercaptopropionic acid (page 178, last two paragraphs) but they do not teach the second end group of the self-assembling molecule is a sulfonate. However, Backhaus et al teach a preferred method for modifying an electrode

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surface to receive a sample liquid comprises modifying the electrode surface with an alkyl linker group comprising a first sulfhydryl end and a second sulfonate end. Specifically, they teach that alkyl chains terminating at one end with a sulfhydryl group bind especially well to gold electrode surfaces and when terminating at the other end with a sulfonate group (SO_4^{-2}) or carboxyl group (CO_2^{-1}) provide a hydrophilic surface as preferred for receiving a sample liquid (Backhaus et al, Column 7, lines 37-40 and 45-49). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify working electrode of McAleer et al by modifying the electrode with mercaptopropionic acid as taught by Mizutani et al to thereby provide a test strip having a rapid response, high sensitivity and high stability for the expected benefit of rapid, sensitive detection over periods of two or more months (Mizutani et al, Abstract). The skilled artisan would have been further motivated to modify the carboxyl group in the mercaptopropionic acid of Mizutani et al by replacing the carboxyl group with a sulfonate group based on the teaching of Backhaus et al wherein a surface modifier comprising a sulfonate and sulfhydryl is preferred because a hydrophilic is desired for receiving sample liquids (Column 7, lines 38-40) and based on the -2 charge of the sulfonate having increased hydrophilic properties. Therefore, the skilled artisan would have been motivated to apply the sulfonate group (SO_4^{-2}) to the surface modification of Mizutani et al to thereby increase the hydrophilic properties of the surface for the expected benefit increasing interaction with an aqueous sample e.g. body fluid samples as suggested by Backhaus (Column 7, lines 39-40).

Regarding Claim 2, McAleer et al teach the test strip wherein the electrode comprises a metal selected from the group consisting of gold, silver and carbon (Column 3, lines 55-58). Mizutani et al teach the similar test strip wherein the electrode comprises gold (page 174, last paragraph, line 1). Backhaus et al teach the similar test strip wherein the electrode comprises gold (Column 4, lines 29-48)

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Regarding Claim 3, McAleer et al teach the test strip wherein the electrode comprises gold (Column 3, lines 55-58). Mizutani et al teach the similar test strip wherein the electrode comprises gold (page 174, last paragraph, line 1). Backhaus et al teach the similar test strip wherein the electrode comprises gold (Column 4, lines 29-48).

Regarding Claim 4, McAleer et al teach the test strip wherein the surface is modified (Column 4, lines 4-26) but they do not teach the surface is modified with $\text{HS}-(\text{CH}_2)_n\text{SO}_3\text{Y}$. Mizutani et al teach the similar method wherein the surface of the working electrode is modified with $\text{HS}-(\text{CH}_2)_n\text{CO}_2\text{Y}$ i.e. mercaptopropionic acid (page 174, last paragraph) wherein the mercaptopropionic acid modification layer provided a rapid response with high sensitivity and high stability (page 178, last two paragraphs) but they do not teach the surface is modified with $\text{HS}-(\text{CH}_2)_n\text{SO}_3\text{Y}$. However, Backhaus et al teach a preferred method for modifying an electrode surface to receive a sample liquid comprises modifying the electrode surface with an alkyl linker group comprising a first sulfhydryl end and a second sulfonate end. Specifically, they teach that alkyl chains terminating at one end with a sulfhydryl group bind especially well to gold electrode surfaces and when terminating at the other end with a sulfonate group (SO_4^{-2}) or carboxyl group (CO_2^{-1}) provide a hydrophilic surface as preferred for receiving a sample liquid (Backhaus et al, Column 7, lines 37-40 and 45-49). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify working electrode of McAleer et al by modifying the electrode with mercaptopropionic acid as taught by Mizutani et al to thereby provide a test strip having a rapid response, high sensitivity and high stability for the expected benefit of rapid, sensitive detection over periods of two or more months (Mizutani et al, Abstract). The skilled artisan would have been further motivated to modify the carboxyl group in the mercaptopropionic acid of Mizutani et al by replacing the carboxyl group with a sulfonate group based on the teaching of Backhaus et al wherein a surface modifier comprising a sulfonate and sulfhydryl is preferred because a hydrophilic is desired for receiving sample liquids (Column 7, lines 38-40) and based on the -2 charge of the

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sulfonate having increased hydrophilic properties. Therefore, the skilled artisan would have been motivated to apply the sulfonate group (SO_4^{2-}) to the surface modification of Mizutani et al to thereby increase the hydrophilic properties of the surface for the expected benefit increasing interaction with an aqueous sample e.g. body fluid samples as suggested by Backhaus (Column 7, lines 39-40).

Regarding Claim 5, McAleer et al teach the test strip wherein at least one enzyme comprises an oxidizing enzyme (Column 2, lines 53-57). Additionally, Mizutani et al teach the similar test strip wherein at least one enzyme comprises an oxidizing enzyme (page, 174, last paragraph-page 175, first paragraph).

Regarding Claim 6, McAleer et al teach an electrochemical test strip comprising: a reaction zone defined by opposing working and reference electrodes separated by a spacer layer wherein at least one of the electrodes has a surface modified with a homogenous surface modification layer; and a redox reagent system in said reaction zone (Column 2, lines 39-57) wherein said redox reagent system comprises enzymes and a mediator (i.e. multiple copies of the glucose oxidase, Column 4, line 58-Column 5, line 2) but they do not teach the modification layer comprises molecules having formula $\text{HS}-(\text{CH}_2)_n-\text{SO}_3\text{Y}$. Mizutani et al teach a similar test strip comprising a reaction zone defined by working and reference electrodes, wherein the working electrode has a surface modified with $\text{HS}-(\text{CH}_2)_n-\text{CO}_2\text{Y}$ i.e. mercaptopropionic acid (page 174, last paragraph); and a redox reagent system present in said reaction zone comprising enzymes (i.e. multiple copies of the glucose oxidase) and a mediator (page 174, last paragraph-page 175, second paragraph and Fig. 1) wherein the mercaptopropionic acid modification layer provided a rapid response with high sensitivity and high stability (page 178, last two paragraphs) but they do not teach the surface is modified with $\text{HS}-(\text{CH}_2)_n-\text{SO}_3\text{Y}$. However, Backhaus et al teach a preferred method for modifying an electrode surface to receive a sample liquid comprises modifying the electrode surface with an alkyl linker group comprising a first sulfhydryl end and a second sulfonate end. Specifically, they

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teach that alkyl chains terminating at one end with a sulfhydryl group bind especially well to gold electrode surfaces and when terminating at the other end with a sulfonate group (SO_4^{-2}) or carboxyl group (CO_2^{-1}) provide a hydrophilic surface as preferred for receiving a sample liquid (Backhaus et al, Column 7, lines 37-40 and 45-49). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify working electrode of McAleer et al by modifying the electrode with mercaptopropionic acid as taught by Mizutani et al to thereby provide a test strip having a rapid response, high sensitivity and high stability for the expected benefit of rapid, sensitive detection over periods of two or more months (Mizutani et al, Abstract). The skilled artisan would have been further motivated to modify the carboxyl group in the mercaptopropionic acid of Mizutani et al by replacing the carboxyl group with a sulfonate group based on the teaching of Backhaus et al wherein a surface modifier comprising a sulfonate and sulfhydryl is preferred because a hydrophilic is desired for receiving sample liquids (Column 7, lines 38-40) and based on the -2 charge of the sulfonate having increased hydrophilic properties. Therefore, the skilled artisan would have been motivated to apply the sulfonate group (SO_4^{-2}) to the surface modification of Mizutani et al to thereby increase the hydrophilic properties of the surface for the expected benefit increasing interaction with an aqueous sample e.g. body fluid samples as suggested by Backhaus (Column 7, lines 39-40).

Regarding Claim 7, McAleer et al is silent regarding the volume of the reaction zone. Additionally, Mizutani et al is silent regarding the volume of the reaction zone. However, Backhaus et al teach that a sample volume between 0.1 and 10 μl is preferred because analytical methods optimally uses small sample quantities (Column 2, lines 34-38). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the sample volume preferred by Backhaus et al to the reaction zone volume in the methods of McAleer et al and Mizutani et al and to provide reaction zone volumes of between 0.1 and 10 μl because one skilled in the art would have been motivated to minimize

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reaction zone volumes to thereby minimize sample volumes for the expected benefit of optimizing sample analysis as taught by Backhaus et al.

Regarding Claim 8, McAleer et al teach the test strip wherein the electrode comprises gold (Column 3, lines 55-58). Mizutani et al teach the similar test strip wherein the electrode comprises gold (page 174, last paragraph, line 1). Backhaus et al teach the similar test strip wherein the electrode comprises gold (Column 4, lines 29-48).

Regarding Claim 9, McAleer et al teach the test strip wherein at least one enzyme comprises an oxidizing enzyme (Column 2, lines 53-57). Additionally, Mizutani et al teach the similar test strip wherein at least one enzyme comprises an oxidizing enzyme (page, 174, last paragraph-page 175, first paragraph).

Regarding Claim 10, McAleer et al teach the test strip wherein the oxidizing enzyme is a glucose oxidizing enzyme (Column 2, lines 53-57). Additionally, Mizutani et al teach the similar test strip the oxidizing enzyme is a glucose oxidizing enzyme (page, 174, last paragraph-page 175, first paragraph).

Regarding Claim 11, McAleer et al teach the test strip wherein the surface is modified (Column 4, lines 4-26) but they do not teach the surface is modified with $\text{HS}-(\text{CH}_2)_n-\text{SO}_3\text{Y}$. Mizutani et al teach the similar method wherein the surface of the working electrode is modified with $\text{HS}-(\text{CH}_2)_n-\text{CO}_2\text{Y}$ i.e. mercaptopropionic acid (page 174, last paragraph) wherein the mercaptopropionic acid modification layer provided a rapid response with high sensitivity and high stability (page 178, last two paragraphs) but they do not teach the surface is modified with $\text{HS}-(\text{CH}_2)_n-\text{SO}_3\text{Y}$. However, Backhaus et al teach a preferred method for modifying an electrode surface to receive a sample liquid comprises modifying the electrode surface with an alkyl linker group comprising a first sulfhydryl end and a second sulfonate end. Specifically, they teach that alkyl chains terminating at one end with a sulfhydryl group bind especially well to gold electrode surfaces and when terminating at the other end with a sulfonate group (SO_4^{2-}) or carboxyl group (CO_2^{-1}) provide a hydrophilic surface as preferred for receiving a sample

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liquid (Backhaus et al, Column 7, lines 37-40 and 45-49). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify working electrode of McAleer et al by modifying the electrode with mercaptopropionic acid as taught by Mizutani et al to thereby provide a test strip having a rapid response, high sensitivity and high stability for the expected benefit of rapid, sensitive detection over periods of two or more months (Mizutani et al, Abstract). The skilled artisan would have been further motivated to modify the carboxyl group in the mercaptopropionic acid of Mizutani et al by replacing the carboxyl group with a sulfonate group based on the teaching of Backhaus et al wherein a surface modifier comprising a sulfonate and sulfhydryl is preferred because a hydrophilic is desired for receiving sample liquids (Column 7, lines 38-40) and based on the -2 charge of the sulfonate having increased hydrophilic properties. Therefore, the skilled artisan would have been motivated to apply the sulfonate group (SO_4^{-2}) (e.g. 2-mercaptoethane sulfonic acid) to the surface modification of Mizutani et al to thereby increase the hydrophilic properties of the surface for the expected benefit increasing interaction with an aqueous sample e.g. body fluid samples as suggested by Backhaus (Column 7, lines 39-40).

Regarding Claim 12, McAleer et al teach an electrochemical test strip comprising: a reaction zone defined by opposing working and reference electrodes separated by a spacer layer wherein at least one of the electrodes has a surface modified with a homogenous surface modification layer; and a redox reagent system in said reaction zone (Column 2, lines 39-57) wherein said redox reagent system comprises enzymes and a mediator (i.e. multiple copies of the glucose oxidase, Column 4, line 58-Column 5, line 2) but they do not teach the modification layer comprises 2-mercaptoethane. Mizutani et al teach a similar test strip comprising a reaction zone defined by working and reference electrodes, wherein the working electrode has a surface modified with 3-mercaptopropionic acid (page 174, last paragraph); and a redox reagent system present in said reaction zone comprising enzymes (i.e. multiple copies of the glucose oxidase) and a mediator (page 174, last paragraph-page 175, second paragraph

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and Fig. 1) wherein the mercaptopropionic acid modification layer provided a rapid response with high sensitivity and high stability (page 178, last two paragraphs) but they do not teach the modification layer comprises 2-mercaptoethane. However, Backhaus et al teach a preferred method for modifying an electrode surface to receive a sample liquid comprises modifying the electrode surface with an alkyl linker group comprising a first sulfhydryl end and a second sulfonate end. Specifically, they teach that alkyl chains terminating at one end with a sulfhydryl group bind especially well to gold electrode surfaces and when terminating at the other end with a sulfonate group (SO_4^{-2}) or carboxyl group (CO_2^{-1}) provide a hydrophilic surface as preferred for receiving a sample liquid (Backhaus et al, Column 7, lines 37-40 and 45-49). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify working electrode of McAleer et al by modifying the electrode with mercaptopropionic acid as taught by Mizutani et al to thereby provide a test strip having a rapid response, high sensitivity and high stability for the expected benefit of rapid, sensitive detection over periods of two or more months (Mizutani et al, Abstract). The skilled artisan would have been further motivated to modify the carboxyl group in the mercaptopropionic acid of Mizutani et al by replacing the carboxyl group with a sulfonate group based on the teaching of Backhaus et al wherein a surface modifier comprising a sulfonate and sulfhydryl is preferred because a hydrophilic is desired for receiving sample liquids (Column 7, lines 38-40) and based on the -2 charge of the sulfonate having increased hydrophilic properties. Therefore, the skilled artisan would have been motivated to apply the sulfonate group (SO_4^{-2}) (e.g. 2-mercaptoethane sulfonic acid) to the surface modification of Mizutani et al to thereby increase the hydrophilic properties of the surface for the expected benefit increasing interaction with an aqueous sample e.g. body fluid samples as suggested by Backhaus (Column 7, lines 39-40).

Regarding Claim 13, McAleer et al is silent regarding the volume of the reaction zone. Additionally, Mizutani et al is silent regarding the volume of the reaction zone. However, Backhaus et al teach that a sample volume between 0.1 and 10 μl is preferred because

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analytical methods optimally uses small sample quantities (Column 2, lines 34-38). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the sample volume preferred by Backhaus et al to the reaction zone volume in the methods of McAleer et al and Mizutani et al and to provide reaction zone volumes of between 0.1 and 10 μ l because one skilled in the art would have been motivated to minimize reaction zone volumes to thereby minimize sample volumes for the expected benefit of optimizing sample analysis as taught by Backhaus et al.

Regarding Claim 14, McAleer et al teach the test strip wherein the electrode comprises gold (Column 3, lines 55-58). Mizutani et al teach the similar test strip wherein the electrode comprises gold (page 174, last paragraph, line 1). Backhaus et al teach the similar test strip wherein the electrode is gold (Column 4, lines 29-43).

Regarding Claim 16, McAleer et al teach a method for determining the concentration of an analyte in a physiological sample comprising: applying the sample to an electrochemical test strip comprising a reaction zone defined by opposing working and reference electrodes and a redox reagent system; detecting an electrical signal in said reaction zone; and relating the detected signal to the amount of analyte in the sample (Example 4, Column 6, lines 33-57) but they do not teach but they do not teach one of the electrodes comprises a modification layer comprises self assembling molecules having a first sulfhydryl end group and a second sulfonate end group. Mizutani et al teach a similar method comprising a reaction zone defined by working and reference electrodes, wherein the working electrode has a surface modified with a homogenous surface modification layer made up of self assembling molecules (page 174, last paragraph); and a redox reagent system present in said reaction zone comprising at least one enzyme and a mediator (page 174, last paragraph-page 175, second paragraph and Fig. 1) wherein the self-assembling molecules have a first sulfhydryl end group and a second carboxylic acid end group where said sulfhydryl and carboxylic acid end groups are separated by a lower alkyl linker group i.e. mercaptopropionic acid (page 178, last two paragraphs)but

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they do not teach the second end group of the self-assembling molecule is a sulfonate. However, Backhaus et al teach a preferred method for modifying an electrode surface to receive a sample liquid comprises modifying the electrode surface with an alkyl linker group comprising a first sulfhydryl end and a second sulfonate end. Specifically, they teach that alkyl chains terminating at one end with a sulfhydryl group bind especially well to gold electrode surfaces and when terminating at the other end with a sulfonate group (SO_4^{-2}) or carboxyl group (CO_2^{-1}) provide a hydrophilic surface as preferred for receiving a sample liquid (Backhaus et al, Column 7, lines 37-40 and 45-49). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify working electrode of McAleer et al by modifying the electrode with mercaptopropionic acid as taught by Mizutani et al to thereby provide a test strip having a rapid response, high sensitivity and high stability for the expected benefit of rapid, sensitive detection over periods of two or more months (Mizutani et al, Abstract). The skilled artisan would have been further motivated to modify the carboxyl group in the mercaptopropionic acid of Mizutani et al by replacing the carboxyl group with a sulfonate group based on the teaching of Backhaus et al wherein a surface modifier comprising a sulfonate and sulfhydryl is preferred because a hydrophilic is desired for receiving sample liquids (Column 7, lines 38-40) and based on the -2 charge of the sulfonate having increased hydrophilic properties. Therefore, the skilled artisan would have been motivated to apply the sulfonate group (SO_4^{-2}) to the surface modification of Mizutani et al to thereby increase the hydrophilic properties of the surface for the expected benefit of more accurate detection of analyte concentration within an aqueous sample e.g. physiological sample as suggested by Backhaus (Column 7, lines 39-40).

Regarding Claim 17, McAleer et al teach the method wherein the surface is modified (Column 4, lines 4-26) but they do not teach the surface is modified with $\text{HS}-(\text{CH}_2)_n-\text{SO}_3\text{Y}$. Mizutani et al teach the similar method wherein the surface of the working electrode is modified with $\text{HS}-(\text{CH}_2)_n-\text{CO}_2\text{Y}$ i.e. mercaptopropionic acid (page 174, last paragraph) wherein

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mercaptopropionic acid modification layer provided a rapid response with high sensitivity and high stability (page 178, last two paragraphs) but they do not teach the surface is modified with $\text{HS}-(\text{CH}_2)_n-\text{SO}_3\text{Y}$. However, Backhaus et al teach a preferred method for modifying an electrode surface to receive a sample liquid comprises modifying the electrode surface with an alkyl linker group comprising a first sulfhydryl end and a second sulfonate end. Specifically, they teach that alkyl chains terminating at one end with a sulfhydryl group bind especially well to gold electrode surfaces and when terminating at the other end with a sulfonate group (SO_4^{-2}) or carboxyl group (CO_2^{-1}) provide a hydrophilic surface as preferred for receiving a sample liquid (Backhaus et al, Column 7, lines 37-40 and 45-49). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify working electrode of McAleer et al by modifying the electrode with mercaptopropionic acid as taught by Mizutani et al to thereby provide a test strip having a rapid response, high sensitivity and high stability for the expected benefit of rapid, sensitive detection over periods of two or more months (Mizutani et al, Abstract). The skilled artisan would have been further motivated to modify the carboxyl group in the mercaptopropionic acid of Mizutani et al by replacing the carboxyl group with a sulfonate group based on the teaching of Backhaus et al wherein a surface modifier comprising a sulfonate and sulfhydryl is preferred because a hydrophilic is desired for receiving sample liquids (Column 7, lines 38-40) and based on the -2 charge of the sulfonate having increased hydrophilic properties. Therefore, the skilled artisan would have been motivated to apply the sulfonate group (SO_4^{-2}) to the surface modification of Mizutani et al to thereby increase the hydrophilic properties of the surface for the expected benefit of more accurate detection of analyte concentration within an aqueous sample e.g. physiological sample as suggested by Backhaus (Column 7, lines 39-40).

Regarding Claim 18, McAleer et al teach the method wherein the surface is modified (Column 4, lines 4-26) but they do not teach the surface is modified with mercaptoethane sulfonic acid. Mizutani et al teach the similar method wherein the surface of the working

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electrode is modified with mercaptopropionic acid (page 174, last paragraph) wherein the mercaptopropionic acid modification layer provided a rapid response with high sensitivity and high stability (page 178, last two paragraphs) but they do not teach the surface is modified with mercaptoethane sulfonic acid. However, Backhaus et al teach a preferred method for modifying an electrode surface to receive a sample liquid comprises modifying the electrode surface with an alkyl linker group comprising a first sulfhydryl end and a second sulfonate end. Specifically, they teach that alkyl chains terminating at one end with a sulfhydryl group bind especially well to gold electrode surfaces and when terminating at the other end with a sulfonate group (SO_4^{-2}) or carboxyl group (CO_2^{-1}) provide a hydrophilic surface as preferred for receiving a sample liquid (Backhaus et al, Column 7, lines 37-40 and 45-49). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify working electrode of McAleer et al by modifying the electrode with mercaptopropionic acid as taught by Mizutani et al to thereby provide a test strip having a rapid response, high sensitivity and high stability for the expected benefit of rapid, sensitive detection over periods of two or more months (Mizutani et al, Abstract). The skilled artisan would have been further motivated to modify the carboxyl group in the mercaptopropionic acid of Mizutani et al by replacing the carboxyl group with a sulfonate group based on the teaching of Backhaus et al wherein a surface modifier comprising a sulfonate and sulfhydryl is preferred because a hydrophilic is desired for receiving sample liquids (Column 7, lines 38-40) and based on the -2 charge of the sulfonate having increased hydrophilic properties. Therefore, the skilled artisan would have been motivated to apply the sulfonate group (SO_4^{-2}) (e.g. 2-mercaptoethane sulfonic acid) to the surface modification of Mizutani et al to thereby increase the hydrophilic properties of the surface for the expected benefit of more accurate detection of analyte concentration within an aqueous sample e.g. physiological samples as suggested by Backhaus (Column 7, lines 39-40).

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Regarding Claim 19, McAleer et al teach the method wherein the analyte is glucose (Column 2, lines 39-43). Mizutani et al teach the similar method wherein the analyte is glucose (page 177, first and second paragraph and Fig. 3 and 4). Backhaus et al teach the similar method wherein the analyte is glucose (Example 1, Column 10, line 50-Column 11, line 11).

Regarding Claim 20, McAleer et al teach the method wherein the redox reagent system comprises a glucose oxidizing enzyme (Column 2, lines 39-43). Mizutani et al teach the similar method wherein the redox reagent system comprises a glucose oxidizing enzyme (page 175, left column, first paragraph and Fig. 1).

Regarding Claim 26, McAleer et al teach the test strip is present in an automated instrument i.e. glucose test meter (Column 3, lines 48-53). Mizutani et al also teach the similar test strip is present in an automated instrument i.e. potentiostat (page 175, first full paragraph). Backhaus et al also teach the similar test strip is present in an automated instrument e.g. spectrophotometer (Column 6, lines 3-23). The claims are given the broadest reasonable interpretation consistent with the claim language and specification wherein the automate instrument is not defined or described by structural components and/or a structure-function relationship. Therefore, given the broadest reasonable interpretation of the claim, the "automated instrument" encompasses the glucose test meter of McAleer et al; encompasses the potentiostat of Mizutani et al; and encompasses the spectrophotometer of Backhaus et al.

Regarding Claim 27, McAleer et al teach the method employs an automated instrument i.e. glucose test meter (Column 3, lines 48-53). Mizutani et al also teach the similar method employs an automated instrument i.e. potentiostat (page 175, first full paragraph). Backhaus et al also teach the similar method employs an automated instrument e.g. spectrophotometer (Column 6, lines 3-23). The claims are given the broadest reasonable interpretation consistent with the claim language and specification wherein the automate instrument is not defined or described by structural components and/or a function-function

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relationship. Therefore, given the broadest reasonable interpretation of the claim, the "automated instrument" encompasses the glucose test meter of McAleer et al; encompasses the potentiostat of Mizutani et al; and encompasses the spectrophotometer of Backhaus et al.

7. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over McAleer et al (U.S. Patent No. 5,708,247, issued 13 January 1998) in view of Mizutani et al (Analytica Chimica Acta, 1998, 364: 173-179) and Backhaus et al (U.S. Patent No. 5,869,001, issued 9 February 1999) as applied to claim 12 above, and further in view of Pritchard et al (U.S. Patent No. 5,762,770, issued 9 June 1998)

Regarding Claim 15, McAleer et al teach an electrochemical test strip comprising: a reaction zone defined by opposing working and reference electrodes separated by a spacer layer wherein at least one of the electrodes has a surface modified with a homogenous surface modification layer; and a redox reagent system in said reaction zone (Column 2, lines 39-57) wherein said redox reagent system comprises enzymes and a mediator (i.e. multiple copies of the glucose oxidase, Column 4, line 58-Column 5, line 2) wherein the electrode is gold (Column 3, line 55-58) but they do not teach the electrode is a palladium electrode. Mizutani et al teach a similar test strip (page 174, last paragraph-page 175, second paragraph and Fig. 1) wherein the electrode is gold (page 174, last paragraph) but they do not teach a palladium electrode. However, palladium electrodes were well known in the art at the time the claimed invention was made as taught by Pritchard et al who teach a similar electrochemical test strip. Specifically, Prichard et al teach their similar test strip comprising a reaction zone defined by opposing working and reference electrodes and a redox reagent system comprising at least one enzyme and a mediator (Column 2, line 64-Column 3, line 15) wherein the preferred working electrode is palladium. They teach palladium is preferred because palladium is difficult to

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oxidize and because it is an inexpensive noble metal (Column 3, lines 33-36). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the palladium electrode to the electrodes of McAleer et al and Mizutani et al to thereby utilize an inexpensive electrode which resists oxidation in the redox reactions of McAleer et al and Mizutani et al. Specifically, one skilled in the art would have been motivated to utilize a palladium electrode in the redox methods because the electrode resists oxidation and therefore would function over a longer period of time. Therefore, skilled artisan would be further motivated to utilize a palladium electrode in the methods of McAleer et al and Mizutani et al based on lower cost and longer life for the expected benefit of economy of cost and time as taught by Pritchard et al (Column 3, lines 33-36).

Conclusion

8. No claim is allowed.
9. Please note that the examiner's Art Unit has changed from 1655 to 1634.
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
February 14, 2002